

REMARKS

Responsive to the lack of unity determination imposed in the Official Action mailed June 14, 2007, applicants hereby provisionally elect Group I and Species C27S K51T R55L G79A (SEQ ID NO: 44), which corresponds to a mutant with 4 mutations located in all of regions 2, 4 and 5, with traverse.

The grounds for traversal are as follows.

According to the Official Action, the common technical feature of Group I-V is a mutant HIV-1 Tat protein comprising at least two mutations in the region between amino acid position 49 and 57, and/or in the region between amino acid position 88 and 92, or in the RGD motif. The Official Action states that the claimed invention lacks unity of invention in view of SIDEROVSKI, which discloses HIV-1 virus Tat-protein mutants comprising at least two mutations.

However, SIDEROVSKI stands in contrast to the claimed invention. SIDEROVSKI relates to a method for the random construction of tat mutagenized genes. This method leads to the synthesis of a random mutagenized Tat protein, yielding an average of 10.9 amino-acid changes per full-length protein (see p. 5314, 2nd column). However, as it is a random method, one skilled in the art cannot be sure or necessarily say that the synthesized proteins comprise at least two mutations in the above-identified regions of Tat-protein.

Moreover, the mutants obtained by SIDEROVSKI comprise different kind of mutations, namely random nucleotide substitutions, single nucleotide insertions, point deletions and gross deletions (p. 5318, 1st column). The claimed invention relates to mutations that represent a substitution of one amino acid for another (see claim 1).

The tat gene used by SIDEROVSKI encodes an 86 amino-acid Tat protein (see p. 5313, 2nd column). The mutants of the present invention generally relate to 101 amino acids. Furthermore, if the consensus Tat protein sequences used in SIDEROVSKI and in the present invention are compared, one can observe that the region between amino acid positions 88 and 92 are different.

These differences are believed to be in part due to the fact that SIDEROVSKI studies regions of the Tat protein to determine each region's biological activity. SIDEROVSKI demonstrate that 75% of amino-acid changes are present in the C-terminal halves of the encoded proteins. This suggests the existence of a selection pressure to avoid N-terminal mutations (see p. 5318, 1st column). Indeed, it appears that the basic-rich TAR-binding domain (aa 49-57) is tolerant to substitution (provided a threshold level of basic charge and arginine residues are present; see p. 5318, 2nd column). Furthermore, there is a threshold of tolerance to multiple changes within the core

domain (aa 32-47), without a complete loss of biological activity of the protein (see p. 5318, 2nd column).


In view of the above, applicants submit that SIDEROVSKI fails to support the lack of unity determination set forth in the Official Action.

Thus, applicants respectfully request a search and examination of all of the pending claims in their full scope.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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